REMARKS

1. Interview on 16 October 2007

The helpfulness and courtesies extended by the Examiner during the interview of 16 October 2007 are appreciated. The rejections under 35 U.S.C. § 112 were discussed, including the issue raised by the Examiner about whether the structure of anakinra was known at the time of filing the present application. No agreement was reached regarding allowance of the claims.

2. Removal of Finality of the Office Action

On December 3, 2007, Applicant filed a Request/Petition for removal of the finality of the outstanding Office Action. It is also noted that while page 1 of the Office Action indicates in box 2(a) that the Office Action is "Final", but the end of the Office Action does not include the standard form paragraphs for a final Office Action. It would, therefore, appear that the indication on page 2 of the Office Action as being "Final" was in error. In a telephone conversation with the Examiner on December 21, 2007, the undersigned was advised that the Office Action should have been a non-final Office Action because it included a new prior art rejection. In a telephone conversation on January 23, 2007, the Examiner advised that an Interview Summary Record form would be issued to explain the situation. Therefore, Applicant requests that the file be clarified to indicate that the outstanding Office Action is indeed a non-final Office Action.

3. Rejection Under 35 U.S.C. § 112 (New Matter)

Claims 15-21 have been rejected under 35 U.S.C. § 112, 1st paragraph, as allegedly containing new matter. This rejection is respectfully traversed.

First of all, the basis for the Examiner's rejection is the dosage range recited in claims 17 and 20-21. Claims 15, 16 and 18 do not recite any dosage ranges, either directly or indirectly, so the new matter rejection is clearly improper with respect to those claims.

With respect to the remaining claims, Applicant submits that the recitation of the dosage range of "0.1 to 1000mg" does not represent new matter because it is clearly supported by the Specification. In particular, page 13, lines 13-15, specifically describe the claimed dosage range as being useful for medicaments for parenteral use, a preferred method of administration for the compounds of the present invention (see for example page 12, lines 23-30). Accordingly, reconsideration and withdrawal of the rejection are requested.

4. Rejections Under 35 U.S.C. § 112 (Written Description)

Claims 15-21 have been rejected under 35 U.S.C. § 112, 1st paragraph (written description). This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The basis for the Examiner's rejection appears to be that "instant claims 15-21" directed to a method for treating type-2 diabetes by administering a medicament comprising anakinra do not "disclose any identifying structural characteristics of anakinra". Applicant first of all submits that the Examiner's alleged criticism is no basis at all for rejecting the claims for alleged lack of written description. The legal issue for purposes of written description is whether the Specification "reasonably conveys to the artisan that the Inventor had possession at the time (the filing date) of the later claimed subject matter". *Ralston Purina Co. v. Far-mar Co.*, 227 USPQ 177, 179 (Fed Cir. 1985). The present application at, for example, the first full paragraph on page 12, clearly describes the use of anakinra, and the commercially available medicament Kineret®, and this disclosure clearly provides sufficient written description support for the claims.

During the interview of October 16, 2007, the Examiner explained that the basis for this rejection is based on a concern of whether the structure of anakinra was known to those skilled in the art at the time of filing the present application. Applicant submits that anakinra was a well known compound as of the filing date of the present application as evidenced by, at least, the following:

1. Exhibit 1 is a product description for Kineret which is the commercially available form of anakinra available through Amgen.
2. Exhibits 2 and 3 are publications in *Nature*, Vol. 343 in 1990 which provide the partial N-terminal sequence (Exhibit 2) and the full length sequence (Exhibit 3) for the IL-1ra.
3. Exhbit 4 to *Cohen et al.* reports on the results of tests on the treatment of rheumatoid arthritis with anakinra, and specifically notes that anakinra is a recombinant human form of the IL-1ra which had recently been approved for the treatment of rheumatoid arthritis (see page 615, left hand column, 2nd paragraph).

Moreover, despite the Examiner's rejection of the claims for alleged lack of written description, the Examiner himself cites U.S. Patent 6,294,170 B1 to *Boone et al.* as disclosing the full length protein sequence (SEQ ID NO. 2).

It is clear, therefore, the Examiner's written description rejection is without basis, and should be withdrawn.

5. Rejections Under 35 U.S.C. § 112 (Enablement)

Claims 15-21 have been rejected under 35 U.S.C. 112, 1st paragraph, for alleged lack of sufficient enablement. This rejection is respectfully traversed. Reconsideration and withdrawal are requested.

The Examiner appears to have two points of alleged criticisms: (a) the allegation that the Specification only provides enablement for *in vitro* methods, and (b) the Specification allegedly does not enable "prophylactic".

(A) The Specification Fully Enables *In Vivo* Methods

The Examiner first urges that the application is not enabled "because the disclosure of anakinra in the specification does not disclose any identifying structural characteristics of anakinra" (see the sentence bridging pages 7 and 8 of the Office Action). This matter has been addressed above with respect to the written description rejection and Applicant believes that this aspect of Examiner's enablement rejection has been similarly overcome.

The Examiner next urges that the application does not enable an *in vivo* method "because the specification does not teach how to use anakinra or anakinra with PDTC in a medicament without undo experimentation with a treatment of a disease in an animal" (see page 8, lines 14-16 of the Office Action, emphasis in original).

First of all, the Specification at pages 11-13 clearly describe the method of the invention for treating type-2 diabetes by administering IL-1ra, including anakinra, to animals, including humans, and that IL-1ra can be administered alone or in combination with PDTC.

In addition, page 22-28 describes a clinical study in humans for the treatment of type-2 diabetes with IL-1ra. While this description is in the "future tense" as a proposed study, it still provides more than sufficient enablement for one skilled in the art to practice the presently claimed invention.

Indeed, results of such a clinical study were published subsequent to filing of the present application, and those results are reported in the attached publication by *Larsen et al.* in the *New England Journal of Medicine* (Exhibit 5). Applicant submits that the results reported in the *Larsen et al.* publication show that the method of the present invention indeed works *in vivo* as described in the present application, and shows that the description in the present application was indeed fully enabling to one skilled in the art.

(B) Prophylactic Treatment

In both the Office Action and the Interview of October 16, 2007 the Examiner raised concerns about use of the term "prophylactically" in claim 15. While Applicant is aware of the USPTO standard reluctance to allow claims that encompass "prophylactic" treatment, Applicant submits that such claims are entirely proper in the present case. Enclosed as Exhibit 6, is a publication to *Maedler et al.* (which includes the present inventor as a co-author) which reports the results of tests on the use of IL-1ra to protect cultured human islets from the deleterious effects of high glucose. As shown in, for example figure 4g, IL-1ra prevented human β-cell apoptosis at high glucose concentrations, evidencing the protecting role of anakinra in preventing type-2 diabetes. In other words, these results show the prophylactic benefit of the method of the present invention, as well as the benefit in preventing type-2 diabetes disease progression.

In addition, Exhibit 7 is an abstract of an article/presentation by *Sauter et al.* at the American Diabetes Association meeting in 2007 which also reports on tests which show that the treatment with IL-1ra in combination with a high fat diet prevented the onset of diabetic symptoms – i.e. the treatment had a prophylactic effect.

Applicant submits that the above arguments and evidence have rebutted each and every one of the Examiner's objections, so that the rejections under 35 U.S.C. § 112, 1st paragraph, should be withdrawn.

6. Claim Rejections – Prior Art Under 35 U.S.C. § 103

Claims 15-17 have been rejected under 35 U.S.C. 103(a) over *Boone et al.* (U.S. Patent 6,294,170) in view of *Thompson et al.* (U.S. Patent 6,159,460). This rejection is respectfully traversed. Reconsideration and withdrawn thereof are requested.

In making the rejection, the Examiner notes that *Boone et al.* teach the use of anakinra for the treatment of "interleukin-1 mediated diseases" including "diabetes (e.g., insulin diabetes)". However, *Boone et al.* says nothing at all about the use of anakinra for the treatment of type-2 diabetes. The differences between the two types of diabetes are significant, and a treatment useful for one type of diabetes cannot be considered *prima facie* obvious for the use in treating the other type of diabetes.

The term "insulin diabetes" as utilized in *Boone et al.* refers exclusively to type-1 diabetes – i.e. insulin dependent diabetes. Type-1 diabetes is an auto-immune disease with the involvement of cytokines, including interleukin-1.

The *Boone et al.* reference cited by the Examiner which relates to treatment of insulin diabetes is completely silent with respect to the use of anakinra for type-2 diabetes. Prior to the present invention there was no indication that type-2 diabetes was related to interleukin-1. Indeed, at that time type-2 diabetes was considered a different disease, unrelated to auto-immunity or auto-inflammatory processes. Therefore, prior to the present invention there was no motivation for one skilled in the art to consider treating type-2 diabetes with interleukin-1 receptor antagonists such as anakinra. Indeed, it was surprising to the present inventor to find that interleukin-1 was implicated in type-2 diabetes.

Thompson et al., cited by the Examiner, similarly only refers to the treatment of interleukin-1 mediated diseases, including insulin diabetes (column 2, line 46), and is silent with regards to any treatment of type-2 diabetes.

For the above reasons Applicant submits that the Examiner's cited combination of references does not establish a *prima facie* case of obviousness. Accordingly, the Examiner's rejection should be withdrawn.

In view of the above, Applicant submits that all of the Examiner's rejections have been overcome, so that this application should now be in condition for allowance. Early action to that effect is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson Reg. No. 30,330 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

By: _____

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